REMARKS

Reconsideration and withdrawal of the rejections of this application and consideration and entry of this paper are respectfully requested in view of the herein remarks and accompanying information, which place the application in condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 1, 9, 21 and 26-39 are pending. Claims 9 and 29-39 are amended without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents.

No new matter is added. Support for the amended claims is found throughout the specification.

It is submitted that these claims are patentably distinct from the references cited by the Examiner, and that these claims are in full compliance with the requirements of 35 U.S.C. §112. The amendments of the claims herein are not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112; but rather the amendments are made simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that the herewith amendments should not give rise to any estoppel, as the herewith amendments are not narrowing amendments.

Abstract of the Disclosure

The application was objected to for not containing an Abstract on a separate sheet. An Abstract on a separate sheet is attached to this Amendment, obviating the objection.

Title of the Invention

The title of the invention was objected to as allegedly not being descriptive. The title has been amended as suggested by the Examiner.

Claim Objections

Claims 9 and 29-39 were objected to as allegedly being drawn to non-elected subject matter. These claims have been amended to recite SEQ ID NO:7, rendering the objection moot.

II. THE REJECTIONS UNDER §112, FIRST PARAGRAPH, ARE OVERCOME

The Application Contains Adequate Written Description

Claims 1, 21, 26-31, 33-35 and 37-39 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking adequate written description. The rejection is traversed.

At page 3, the Office Action contends that the application "describes a single genomic sequence ... that encodes glucan lyase", and that it "does not describe other DNA sequences that encode glucan lyase, especially those that have 75%, 85% or 90% sequence homology to the sequence set forth in SEQ ID NO: 7." To the contrary, the application does describe other DNA sequences that encode glucan lyase, and designates them SEQ ID NOs: 8-12. As stated in the Office Action mailed on October 9, 2001, these sequences encode distinct glucan lyases. Therefore, there are certainly enough representative species disclosed in the application to justify a claim to the genus of glucan lyases. The Office Action also contends that the breadth of the claims is not supported by the specification because the claims encompass nucleic acids that are homologous to that represented by SEQ ID NO: 7. Applicants do claim a genus, however, there is more than adequate support for the claims.

Enzo Biochem Inc. v. Gen-Probe Inc. (Fed. Cir. 01-1230; July 2002) holds that a functional description of genetic material may be sufficient to satisfy the written description requirement of 35 U.S.C. §112, since the requirement can be met by showing that invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, including functional characteristics, when coupled with known or disclosed correlation between function and structure. And according to MPEP 2163 IIA3(a)ii, to support a claim to a genus requires:

> sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Applicants have clearly provided relevant, identifying characteristics in the form of nucleotide sequences. Further, they have provided examples in the application demonstrating the functional properties of the nucleic acid molecules and a correlation between function and structure. For example, in the paragraph beginning on page 10, line 4, the application describes both functional characteristics, *i.e.* that the resultant enzyme has glucan lyase activity, and structural characteristics in the form of sequence homology information. There are reasonable limits regarding what the claimed nucleic acid molecules can comprise. The fact that they are not necessarily required to comprise the entire disclosed sequence does not render them inadequately described.

Furthermore, limiting the Applicants to only the disclosed sequences would unfairly narrow the scope of the invention. For example, other parties could use nucleic acid molecules distinct from SEQ ID NO: 7 that encode a structurally or functionally identical enzyme to practice this very invention, and they would fall outside the literal scope of the claims. Such a consequence is obviously contrary to the intended function of the patenting system.

One skilled in the art could clearly conclude from the application that the Applicants had possession of the claimed invention at the time of filing. Consequently, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first paragraph, are in order, and such relief is requested.

The Specification Is Enabling

Claims 1, 21, 26-31, 33-35 and 37-39 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. The rejection is traversed.

According to the Court of Appeals for the Federal Circuit in the case of *In re Wands*, 8 U.S.P.Q. 2d 1400 (Fed. Cir. 1988),

> Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. **The key word is undue, not experimentation.** The determination of what constitutes undue experimentation in a given case requires the application of standard of reasonableness, having due regard for the nature of the invention and the state of the art. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed ... [Citations omitted].

Id. at 1404.

Against this background, determining whether undue experimentation is required to practice a claimed invention turns on weighing many factors summarized in *In re Wands* (*Id.*). For example, (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples of the invention; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims.

The assertion in the Office Action that the instant invention does not provide enablement for isolation of DNA sequences from a broad category of glucan lyases or their homologues is misplaced because undue experimentation would not exist. Applying *Wands* to the instant facts, it is clear that enablement exists: the amount of direction or guidance presented is high; working examples are clearly present; the relative skill of those in the art is high; and the predictability of the art is also high. Although a person of skill in the art may have to test an enzyme encoded by a nucleotide of a claimed sequence or homologue to determine whether it had glucan lyase activity, the means for doing so are described in the specification, are within the capability of the skilled artisan, and do not constitute undue experimentation.

It is respectfully submitted that adequate guidance is provided to enable the skilled artisan to practice the claimed invention without undue experimentation. Therefore, reconsideration and withdrawal of the U.S.C. § 112, first paragraph rejections are earnestly solicited.

III. THE REJECTIONS UNDER §112, SECOND PARAGRAPH, ARE OVERCOME

Claims 21 and 29-39 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

The Office Action states that the recitation in claim 21 "improving the transformation" is indefinite because it is not clear how the transformation is to be improved. The language presented in claim 21 is standard Jepson language. No further recitation is required in the preamble because what follows (*i.e.* "the improvement comprising") defines the improvement.

Claims 29-39 were rejected because the Office Action alleges that "homology" is an archaic term in the art. As suggested by the Examiner, "homology" has been replaced in the claims by "identity". It should be noted, however, that a search of the USPTO database, from 1996 to the present, for the terms "homology" and "sequence" in the claims, returned 373 patents that used homology in this context. Some of these patents issued as recently as last week, casting doubt on the allegation that the term is "archaic".

Claims 36 was rejected as allegedly lacking sufficient antecedent basis for "the recombinant enzyme". Claims 37 and 38 were rejected as allegedly lacking sufficient antecedent basis for "the enzyme". The base claim of all of these is claim 21, which recites "recombinant enzyme" twice. C 32 also recites "the recombinant enzyme", and claims 29-31, 33-35 and 39 also recite "the enzyme", and these were not included in this rejection. It is submitted that "the

recombinant enzyme" of claims 32 and 36 and "the enzyme" of claims 29-31, 33-35 and 37-39 all find antecedent basis in their common base claim, claim 21.

In view of the foregoing, reconsideration and withdrawal of the Section 112, second paragraph rejections, are requested.

IV. THE REJECTIONS UNDER §103 ARE OVERCOME

Claims 21, 28 and 32-39 were rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Yu *et al.* in view of Perl *et al.* Claims 1, 9, 26, 27 and 29-31 were rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Yu *et al.* in view of Perl *et al.* The cited documents, alone or in combination, fail to disclose, suggest, or motivate a skilled artisan to practice the presently claimed invention. The rejection is respectfully traversed.

The present invention is predicated upon the realization that the anti-oxidant anhydrofructose could be prepared in plants *in situ*. Prior to the present invention, anhydrofructose was produced in microorganisms, such as bacteria, yeast and fungi, and research was focused on large-scale production of anhydrofructose using microorganisms. (See Yu *et al.*)

The state of the law in the Federal Circuit requires that the suggestion or motivation to practice the claimed invention must be present in the cited art, and not gleaned from the Applicant's specification. Further, picking and choosing portions from a plethora of disparate references in a hindsight attempt to formulate an obviousness rejection is prohibited. In the instant case, the only suggestion or motivation to provide for the recombinant expression of glucan-metabolizing enzymes in plants to produce anti-oxidants *in situ* is found in the Applicant's disclosure. A *prima facie* case of obviousness has not been made.

There is no teaching or suggestion in Yu *et al.* that anhydrofructose could or should be produced *in situ* in plants. Once this was envisaged, Applicants agree that there was no difficulty in transforming the plants, however, the invention is the realization that this should be done *in situ* in plants. Thus, the invention lies in solving the problems associated with producing anhydrofructose in microorganisms, the method used prior to the instant invention.

It is asserted on page 7 of the Office Action that it would have been obvious "to modify the invention of Yu *et al.* for production of anhydrofructose by expressing the α-1,4-glucan lyase in a host capable of the starch degradation pathway to transform grape as taught by Perl rather than a cellular organism." Applicants dispute that the Yu reference contemplates the transformation of <u>any</u> host that can produce anhydrofructose, and do not find specific sentences

in the reference to that effect. In fact, Yu *et al.* only relates to the transformation of microorganisms. It has recently been held by the Court of Appeals for the Federal Circuit that an invention cannot be extrapolated from the prior art if it did not, in fact, exist in the prior art. *See, Elan Pharmaceuticals Inc. v. Mayo Foundation for Medical Education and Research*, 64 USPQ 2d 1292, 1297 (Fed. Cir. 2002). In that case, it was ruled that a transgenic mouse containing a mutated gene was a novel invention, in spite of the fact that the gene and methods for making trangenic mice were previously known in the art. By analogy, the transformation of microorganisms by Yu *et al.* cannot be applied to the transformation of plants, as it was not obvious to one of skill in the art that plants could be transformed to produce functional antioxidants, *in situ*.

Prior to the present invention, antioxidants were added as "chemical" additives to foodstuffs, including beverages. For example, antioxidants were used as preservatives in foodstuffs, particularly when the foodstuff comprised fats. In addition, in winemaking, prior to the present invention, sulfur dioxide was added to prevent chemical oxidation reactions. Thus, the sulfur dioxide acts as a chemical additive that stabilizes natural grape aromas and flavors (for example, see pages 1-2 of the specification of the present application).

The addition of chemical additives, such as potentially harmful chemicals (i.e., sulfur dioxide) and chemical antioxidants, to foodstuffs is disadvantageous. Thus, the "problem" overcome by the present invention is the unwanted addition of potentially harmful chemicals and chemical antioxidants to foodstuffs.

The present invention seeks to provide foodstuff, which foodstuff is comprised of a plant or part thereof, to which no "external" chemical antioxidants or additives need be added as preservatives or stabilizers. In other words, the present invention seeks to provide a foodstuff which produces its own antioxidant, namely anhydrofructose, *in situ*.

None of the prior art documents teach or suggest a process for producing a foodstuff, including a plant or part thereof, comprising transforming a plant with a nucleotide sequence encoding a recombinant glucan lyase enzyme which acts on a glucan substrate in said plant to yield the antioxidant anhydrofructose *in situ*, thus circumventing the need to add an antioxidant "externally" to said foodstuff. Thus, the present invention provides for an improvement over prior art practices, i.e. the external addition of chemical additives and antioxidants to foodstuffs.

An advantage of providing an antioxidant, namely anhydrofructose, in a foodstuff is that antioxidants are often taken as nutritional supplements. Thus the production of a foodstuff with *in situ* above-normal levels of an antioxidant - anhydrofructose - may circumvent the need for additional nutritional supplements of antioxidants. In addition, a further advantage is to assist transformation of a plant, e.g. a grape, transformed with a nucleotide sequence encoding glucan lyase, which, *in situ*, produces the antioxidant anhydrofructose.

Perl teaches the role of "external" antioxidants during *Agrobacterium*-mediated transformation of grape. As can be seen on page 645, column 1, line 6 *et seq* of Perl, different antioxidants were added to the co-cultivation medium. In contrast, the transformed grapes of the present invention were prepared following the teachings of Perl, "but wherein the combination of polyvinylpolypyrrolidone and dithiothreitol is optional" (page 23, lines 16-18 of the specification).

Thus, the present invention teaches a transformation method based on Perl, but without the need to add external, chemical antioxidants to the co-cultivation medium. Instead, it was found that, by transforming the grapes with any one of the nucleotide sequences presented as SEQ. ID. No. 7-12 encoding glucan lyase, the transformation was assisted by the *in situ* preparation of the antioxidant anhydrofructose.

The method according to the present invention is not necessarily an improvement over the teaching of Perl, but is rather an alternative means for transforming grape (see page 21, line 13). One improvement presented by the instant invention is that transformation can be assisted without the need to add "external" chemical antioxidants to the co-cultivation medium. That is to say, the difference is that the antioxidant, anhydrofructose, is produced *in situ* in the plant.

It is submitted therefore that none of the cited documents, either alone or in combination, would lead the skilled person to express, in a plant, a recombinant enzyme that acts on a glucan substrate to produce an anti-oxidant. None of the references teach the transformation of a plant with a nucleotide sequence encoding glucan lyase for the *in situ* production of the antioxidant anhydrofructose. In addition none of the prior art documents suggest the expression of glucan lyase in a plant to produce anhydrofructose *in situ* in the plant. Therefore, a further improvement of the instant invention is to produce an antioxidant within a plant/foodstuff and to overcome the need to add external chemicals, particularly external chemical antioxidants, to the foodstuff.

Thus, the claims are novel and inventive over the cited art. Accordingly, reconsideration and withdrawal of the Section 103 rejections are believed to be in order and such action is respectfully requested.

CONCLUSION

As Applicants have presented at least one new claim, if any Office Action issues in the CPA, it cannot be a first Office Action Final Action. However, in view of the remarks and amendments herewith, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date.

Respectfully submitted,

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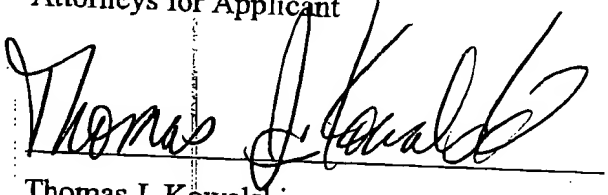

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Version with Markings to Show Changes Made

IN THE TITLE

On page 1, line 1, with the following rewritten title:

A PROCESS FOR PREPARING AN ANTI-OXIDANT IN A PLANT BY TRANSFORMATION WITH GLUCAN LYASE DNA

IN THE CLAIMS

9. (Thrice Amended) In the process according to claim 1, wherein the enzyme is encoded by a nucleotide sequence having [any one of the sequences shown as] SEQ ID NO[s]: 7[-12].

29. (Amended) In the process according to claim 1, wherein the enzyme is encoded by a nucleotide sequence having at least 75% identity[homology] to [any one of] the sequence[s] shown as SEQ ID NO[s]: 7[-12].

30. (Amended) In the process according to claim 1, wherein the enzyme is encoded by a nucleotide sequence having at least 85% identity[homology] to [any one of] the sequence[s] shown as SEQ ID NO[s]: 7[-12].

31. (Amended) In the process according to claim 1, wherein the enzyme is encoded by a nucleotide sequence having at least 90% identity[homology] to [any one of] the sequence[s] shown as SEQ ID NO[s]: 7[-12].

32. (Amended) In the process according to claim 21, wherein the recombinant enzyme is encoded by [any one of] the sequence[s] shown as SEQ ID NO[s]: 7[-12].

33. (Amended) In the process according to claim 21, wherein the enzyme is encoded by a nucleotide sequence having at least 75% identity[homology] to [any one of] the sequence[s] shown as SEQ ID NO[s]: 7[-12].

34. (Amended) In the process according to claim 21, wherein the enzyme is encoded by a nucleotide sequence having at least 85% identity[homology] to [any one of] the sequence[s] shown as SEQ ID NO[s]: 7[-12].

35. (Amended) In the process according to claim 21, wherein the enzyme is encoded by a nucleotide sequence having at least 90% identity[homology] to [any one of] the sequence[s] shown as SEQ ID NO[s]: 7[-12].

36. (Amended) In the process according to claim 28, wherein the recombinant enzyme is encoded by [any one of] the sequence[s] shown as SEQ ID NO[s]: 7[-12].

37. (Amended) In the process according to claim 28, wherein the enzyme is encoded by a nucleotide sequence having at least 75% identity[homology] to [any one of] the sequence[s] shown as SEQ ID NO[s]: 7[-12].

38. (Amended) In the process according to claim 28, wherein the enzyme is encoded by a nucleotide sequence having at least 85% identity[homology] to [any one of] the sequence[s] shown as SEQ ID NO[s]: 7[-12].

39. (Amended) In the process according to claim 28, wherein the enzyme is encoded by a nucleotide sequence having at least 90% identity[homology] to [any one of] the sequence[s] shown as SEQ ID NO[s]: 7[-12].